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APPLICATION NO.	FILING DATE	INVENTOR NAME (LAST, FIRST, MIDDLE)	ATTORNEY NAME (LAST, FIRST, MIDDLE)	ATTORNEY FIRM
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DATE MAILED: 04 04 2003

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Please find below and or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/132,156

Applicant(s)

WITTWER ET AL.

Examiner

Ardin Marschel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 December 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 59-65, 67-76 and 78-90 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 59-65, 67-72, 74-76, 78, 79, and 81-90 is/are rejected.
- 7) ☒ Claim(s) 73 and 80 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

Applicants' arguments, filed 12/3/02, have been fully considered and they have been persuasive to overcome the previous rejections of record. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Upon reconsideration, however, the following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

The cancellation of claims 66 and 77 is acknowledged as being included in amendment E, filed 3/11/02, and inadvertently overlooked due to a lack of a claim cancellation statement which explicitly cited the cancellation of claims 66 and 77, but rather a statement that claims are canceled if not reiterated in said amendment E. It is requested that applicants include an explicit listing of any canceled claims in the future to prevent the overlooking of such cancellation(s).

The newly submitted Declaration, filed 12/3/02, is acceptable.

VAGUENESS AND INDEFINITENESS:

Claims 59, 61-65, 67-69, and 81-90 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 81 cites a method of subjecting a sample...to amplify a nucleic acid. In contrast, the method steps in the claims, as a) and b), lack any reference to either amplification practice or nucleic acid practice. Thus, unclarity exists as to whether the metes and bounds of claim 81 are defined by the preamble or the actually recited claim steps. Clarification via clearer claim wording is requested. This rejection applies also to

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claims 82-89 which depend directly or indirectly from claim 81 due to their dependence and also lacking steps to clarify the above conflict in claim wording.

Claim 81 is additionally vague and indefinite in that the preamble cites the method as being directed to thermal cycling practice but which is not present as a requirement in the actual claim steps. In steps a) and b) in claim 81 the sample temperature is raised and lowered but without any apparent cycling of temperature. Cycling is reasonably interpreted as a repetitive practice but there is nothing repetitive in either of steps a) or b) of claim 81. Thus, unclarity exists as to whether the metes and bounds of claim 81 are defined by the preamble or the actually recited claim steps. Clarification via clearer claim wording is requested. This rejection applies also to claims 82 and 84-89 which depend directly or indirectly from claim 81 due to their dependence and also lacking steps to clarify the above conflict in claim wording.

Similar to claim 81, it is also noted that instant claim 59 contains thermal cycling in the preamble but no cycling is required in the actual claim steps. It is noted that the last two lines of claim 59 define one cycle but that this is not a cycling requirement in the practice of claim 59 as cycling is reasonably interpreted as a repetitive practice. This rejection applies also to claims 61-65 and 67-69 which depend directly or indirectly from claim 59 due to their dependence and also lacking steps to clarify the above conflict in claim wording.

Claim 83 is vague and indefinite in lacking clear antecedent basis for the phrase "the steps" as to which steps are meant of the three steps a), b), and/or c). Clarification via clearer claim wording is requested.

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Claim 90 is vague and indefinite due to lacking clear antecedent basis for "the" amplification products in line 2 therein. No specific antecedent amplification products are cited in claim 70 from which claim 90 depends. Clarification via clearer claim wording is requested.

PRIOR ART:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 81, 83, and 84 are rejected under 35 U.S.C. 102(e)(2) as being clearly anticipated by Mullis et al. (P/N 5,656,493).

Mullis et al. (P/N 5,656,493) describes subjecting a sample to thermal cycling in a PCR procedure in order to amplify nucleic acid(s) as summarized in the abstract. This reference qualifies as prior art relative to the instant application due to its being within a series of continuation applications going back at least to August 22, 1986.

Several descriptions in the reference document various rapid thermal cycling practices as also instantly claimed of which one type of temperature cycling is depicted in Figure 5 for the amplification of nucleic acid. A chill-down rate of an excess of 100 degrees C. per minute is set forth in the reference in column 9, lines 39-42, which computes to a chill-down rate in excess of 1.67 degrees C. per second which is a rate

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specie within the rate of instant claim 81. A specie of a claimed invention is deemed to anticipate such a claimed invention.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 59-62, 64, 65, 67, 68, 70-72, 74-76, 78, 79, 81, 83-86, and 88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mullis et al. (P/N 5,656,493).

Mullis et al. (P/N 5,656,493) describes subjecting a sample to thermal cycling in a PCR procedure in order to amplify nucleic acid(s) as summarized in the abstract. This reference qualifies as prior art relative to the instant application due to its being within a series of continuation applications going back at least to August 22, 1986.

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Several descriptions in the reference document various rapid thermal cycling practices as also instantly claimed of which one type of temperature cycling is depicted in Figure 5 for the amplification of nucleic acid. Columns 13-14 of the reference set forth various time periods and temperatures for the amplification cycles utilized therein. In column 13, lines 1-8, the high temperature incubation for denaturation is described as in the range of 80 – 105 degrees C. In column 13, line 67, through column 14, line 22, the amplification temperature range for thermostable enzyme amplification is described as being 35 – 60 degrees C. In particular, column 14, lines 2-5, an immediate chill-down is described as being performed with dry ice which may be interpreted as approaching a very short chill-down time nearing almost zero time which suggests a short temperature lowering time as required in instant claim 81. Alternatively, the chill-down range is described as occurring in 0.5 to 5 minutes preferably in the reference in column 14, lines 7-9. Thus, a rate of temperature lowering may be reasonably interpreted from these temperature ranges and numbers. The highest rate of numerically defined temperature lowering would be practiced if the highest denaturation temperature (i.e., 105 degrees C.) is present prior to chill-down and the lowest enzyme amplification temperature (i.e., 35 degrees C.) combined with the shortest chill-down time of 0.5 minutes. This results in a temperature lowering rate interpretation of 70 degrees C. in 30 seconds which is a lowering rate of 2.33 degrees C. per second which falls within the rate requirement of instant claim 81. If there is only a 45 (about 42 degrees) C. temperature difference as required in instant claim 85, the rate in the reference would be 1.5 degrees C. per second. It is noted that the dry ice chill-down

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may be at a higher rate but that a numerical evaluation is not set forth in the reference for what is meant by immediate chill-down. A chill-down rate of an excess of 100 degrees C. per minute is set forth in the reference in column 9, lines 39-42, which computes to a chill-down rate in excess of 1.67 degrees C. per second which also is contained within the rate of instant claim 81. It is also acknowledged that the above rate evaluation gives a much slower temperature lowering rate if the smallest temperature difference between the denaturation temperature and the enzyme amplification temperature is utilized with the longest chill-down time of 5 minutes. The above discussion, however, documents the overlapping temperature lowering rates between the instant claim 81 rate and that of the reference. Thus species of practice of temperature cycling wherein the temperature lowering of the reference falls within the range of instant claim 81. A specie as claimed within a generic reference description is deemed to be motivated and suggested as a specie in the reference thus supporting this obviousness type rejection.

It is noted that the temperature rise and fall times are generally in the range of about 0.5 – 5 minutes in said column 13-14 descriptions in the reference. The denaturation temperature time period is described as about 0.5 to four minutes as in column 35, lines 18-24. The enzymatic amplification temperature time period is described in column 38, lines 65-67, as about 0.5 to 40 minutes. It is noted that the time periods for the temperature rise and fall as well as denaturation and enzyme polymerization add to make up a cycle in the reference for the thermal cycling therein for PCR. Each of the four time periods in the reference is described with a lower time

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interval of about 0.5 minutes. Thus, the range of total time for each cycle covers values with the lower limit being "about" 2 minutes or about 120 seconds. One reasonable interpretation of the about language in the instant claims as well as in the reference is that these limitations are functional in nature and thus expand the corresponding times to cover methods which perform the same function with similar times as not exactly defined by the numerical values but rather inclusive of methods which are functionally suggested but with broadly interpreted time periods. This interpretation suggests and motivates the concept that there is an overlap between the instant claim interpretation and that of the PCR methods of the reference including the "about" time interval limitations. It is additionally pointed out that several of the instant claims cite the practice of a "third" temperature but without limiting this temperature to being different from either of the first or second temperatures and thus are included as rejected herein. It is lastly noted that instant claim 61 and 72 are directed to further limitations to a plurality of sample holders. These claims are included as rejected hereinunder because it is deemed obvious to perform an invention as often as desired to obtain the benefits therefrom thus including a plurality of sample holders in a plurality of sample amplifications. It is noted that claims 61 and 72 lack any limitations to distinguish the therein plurality of sample holders from merely being directed to multiple performance samples of the invention of Mullis et al.

Thus, it would have been obvious at the time of the instant invention to perform the PCR of Mullis et al. as functionally rapid to be performed within the instantly broadly

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worded time intervals to result in amplified nucleic acid with a reasonable expectation of success thus resulting in the practice of the instant invention.

Claims 59-62, 64, 65, 67, 68, 70-72, 74-76, 78, 79, 81, 83-86, 88, and 90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mullis et al. (P/N 5,656,493); taken in view of Ward et al. (EP 0,063,879).

The above discussion summarizes the descriptions in Mullis et al. regarding rapid PCR thermocycling. This rejection is directed to embodiments in the instant claims that are present due to their open claim wording and therefore inclusive of fluorescence detection of amplification products as cited specifically in instant claim 90. Mullis et al. lacks specific fluorescence detection of amplification products but does motivate and suggest both radioactive and non-radioactive detection practice of amplification products in column 45, lines 11-26. Mullis et al. specifically motivates and suggests the Ward EP 63,879 procedures of labeling in column 46, lines 8-18.

Ward et al. (EP 0,063,879) describes the substitution of the therein described labeling practice for radioactive labeling on page 9, lines 11-35. The detection of biotin labeled nucleic acids as labeled in the Ward et al. methods is inclusive of fluorescence detection as described on page 29, line 29, through page 30, line 10.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to perform the rapid PCR methods of Mullis et al. motivated to add non-radioactive detection, inclusive of fluorescent detection as set forth in Ward et al. to result in the above listed instant claims which include such fluorescent detection

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practice, specifically as cited in instant claim 90 but present within the remaining listed claims due to their open claim wording.

Claims 73 and 80 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703)308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703)308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703)308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

April 3, 2003

Ardin U Marschel
Ardin U Marschel
Ph.D.